SCIENTIFIC ABSTRACT

Chronic lymphocytic leukemia (CLL) is an accumulative disease of slowly-dividing mature-appearing monoclonal B cells in the blood, marrow, and lymphoid tissues. There is no cure for this disease, which is the most common form of adult leukemia in Western societies, accounting for approximately 30 percent of all leukemias. Therefore, it is extremely important to develop novel therapeutic treatment strategies.

Recognizing that CD40/CD40 ligand (CD154) interactions play a critical role in immune activation, we propose to intravenously administer CLL B cells modified ex vivo with replication defective adenovirus to express a functional and stable chimeric ligand of CD40 (CD154) to stimulate an autologuus anti-leukemia immune response. The objectives of this clinical study are:

Primary Objective:

Assess the toxicities, tolerability, and safety of $1x10^8$, $3x10^8$, and $1x10^9$ autologous Ad-ISF35-transduced CLL B cells given as a single intravenous infusion in up to 18 patients with CLL.

Secondary Objectives:

- Assess the anti-leukemia activity of a single intravenous dose by evaluating reduction in leukemia count, reduction in adenopathy and splenomegaly, and improvement in bone marrow function.
- Assess the quality of life with ISF35 treatment.
- Assess pharmacodynamic endpoints including induction of T cell anti-leukemia immune responses, antibody production against autologous CLL B cells, changes in bystander leukemia cell phenotype including expression of co-stimulatory molecules (CD80 and CD86) and apoptosis-related receptors (CD95 and DR5), expression of intracellular pro- and anti-apoptotic proteins and effector caspases, and changes in plasma cytokine levels.